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MATHEMATICAL MODEL OF THE COMPLICATIONS AND CONTROL OF DIABETES MELLITUS

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ABSTRACT

In this paper, we proposed a model based on the number of diabetics with complications and number of diabetics with and without complications. We analyzed the stability criteria of the model and observed that the complications can be controlled while diabetes persist. We obtained the analytic solution of the system of ordinary differential equation. The limiting case behaviour of each parameter in the analytic solution of the model was studied and interpreted.

KEYWORDS: Diabetes, Complications, Differential Equations

1. INTRODUCTION

Diabetes is a condition that occurs when the normal insulin-glucose-glucagon regulatory mechanism is affected. It is a group of chronic and complex multifactorial diseases characterized by hyperglycaemia [1], [10]. The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity [12]. According to one of the latest International Diabetes Federation report, ≈ 8.3 percent of the global population has diabetes, with this figure expected to rise to ≈ 9.9 by 2030. In addition the International Diabetes Federation has also estimated that several million people have the condition but are unaware of it.

2. COMPLICATIONS OF DIABETES MELLITUS

It is important to understand various complications of diabetes because of its increasing prevalence across the globe. The complications could broadly classified into two, acute and chronic complications.

2. 1 Acute Complications of Diabetes

Acute complications are very serious and strong. They are usually dangerous complications and are always medical emergency. They include the followings:

2. 1. 1 Diabetic Ketoacidosis (DKA)

Low insulin levels cause the liver to turn fatty acid to ketone for fuel (i.e. Ketosis). Elevated levels of ketone bodies in the blood decrease the blood's pH, leading to DKA. The patient in DKA is typically dehydrated and breathing rapidly and deeply. Ketoacidosis can easily become severe enough to cause hypotension, shock, and death.

2. 1. 2 Hyperglycaemia Hyperosmolar State

Hyperosmolar nonketotic state (HNS) shares many symptoms with DKA, but an entirely different origin. In a person with very high blood glucose level (usually considered to be above 300 mg/dl (16mmol/L)), water is osmotically drawn out of cells into the blood and kidneys eventually begin to dump glucose into urine. This results in loss of water and

an increase in blood osmolarity.

2. 1. 3 Hypoglycaemia

Hypoglycaemia, or abnormally low blood glucose, is an acute complication of several diabetes treatments. It is rare otherwise, either in diabetic or non-diabetic patients.

This may be caused by several factors, such as too much or incorrectly timed insulin, too much or incorrectly timed exercise or not enough food (especially glucose containing carbohydrates).

2. 1. 4 Diabetic Coma

Diabetes coma is a medical emergency in which a person with diabetes mellitus is unconscious because of one of the acute complications of diabetes; severe diabetic hypoglycaemia, diabetic ketoacidosis and hyperosmolar nonketotic coma.

2. 1. 5 Respiratory Infections

The immune response is impaired in individuals with diabetes mellitus. Hyperglycaemia both reduces the function of immune cells and increases inflammation. The vascular effects of diabetes also tend to alter lung function, all of which leads to an increase in susceptibility to respiratory infections among individuals with diabetes. Diabetes is associated with a worse disease course and slower recovery from respiratory infections.

2. 1. 6 Periodontal Disease

Diabetes is associated with periodontal disease (gum disease) and may make diabetes more difficult to treat.

2. 2 Chronic Complications of Diabetes

Chronic complications continue for a long time and are not easily cured. Chronic elevation of blood glucose level leads to damage of blood vessels (angiopathy). The resulting problems are grouped under ” micro vascular disease” (due to damage to small blood vessels) and ”macro vascular disease” (due to damage to arteries).

2. 2. 1 Microvascular Complications

2. 2. 1. 1 Diabetic Retinopathy

Diabetic retinopathy is the growth of friable and poor-quality new blood vessels in the retina as well as macular edema (swelling of the macula), which may lead to severe vision loss or blindness. It is responsible for 10,000 new cases of blindness every year in the United States alone [6]. Retinopathy may begin to develop as early as 7 years before the diagnosis of diabetes in patients with type 2 diabetes. It is generally classified as either background or proliferative. Close surveillance for the existence or progression of retinopathy in patients with diabetes is crucial [13].

2. 2. 1. 2 Diabetic Nephropathy

Diabetic nephropathy is the damage to the kidney which can lead to chronic renal failure, requiring dialysis. The pathological changes to the kidney include increased glomerular basement membrane thickness, micro-aneurysm formation, mesangial nodule formation and other changes. Diabetes mellitus is the most cause of adult kidney failure in the developed world.

2. 2. 1. 3 Diabetic Neuropathy

Diabetic neuropathy is the abnormal and decreased sensation, usually starting with the feet but potentially in other nerves, later often finger and hands. It is recognized by the American Diabetes Association (ADA) as "the presence of symptoms and/ or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" [2].

2. 2. 2 Macrovascular Complications

The central pathological mechanism in the macrovascular disease is the process of atherosclerosis, which leads to narrowing of arterial walls throughout the body. They include:

2. 2. 2. 1Coronary Artery Disease

Coronary artery disease leads to angina or myocardial infarction ("heart at- tack"). ADA and American Heart Association recommend that diabetes be considered a coronary artery disease risk equivalent rather than a risk factor [11].

2. 2. 2.2 Stroke and Cardiovascular Disease (CVD)

Diabetes increases the risk that an individual will develop stroke and cardiovascular disease. In fact, CVD accounts for the greatest component of health care expenditures in people with diabetes [11]. Stroke and cardiovascular disease are the primary cause of death in diabetics [9].

2. 2. 2. 3 Diabetic Foot

Diabetic foot is often due to a combination of sensory neuropathy (numbness and insensitivity) and vascular damage. It increases rates of skin ulcers (diabetic foot ulcers) and infection and, in serious cases, necrosis and gangrene. It is why diabetics are prone to leg and foot infections and why it takes longer for them to heal from leg and foot wounds. It is the most common cause of non-traumatic adult amputation, usually of toes and or feet, in the developed world.

3. THE MATHEMATICAL MODEL

Boutayab et al [5] proposed a model on diabetes with complication, and with and without complication which is

$$C'(t) = -(\lambda + \theta)\, C(t) + \lambda N(t) \qquad C(0) = C0 \tag{1}$$

$$N'(t) = I(t) - (\nu + \delta)\, C(t) - \mu N(t) \qquad N(0) = N0 \tag{2}$$

in the present work we have

$$C'(t) = I(t) - (\lambda + \theta)\, C(t) + \lambda N(t) \qquad C(0) = C_0 \tag{3}$$

$$N'(t) = 2I(t) - (\nu + \delta)\, C(t) - \mu N(t) \qquad N(0) = N_0 \tag{4}$$

Where

$$\theta = \gamma + \mu + \nu + \delta \tag{5}$$

$$N(t) = D(t) + C(t) \tag{6}$$

$$N'(t) = D'(t) + C'(t) \tag{7}$$

$$D'(t) = I(t) - (\lambda + \mu)\, D(t) + \gamma C(t) \tag{8}$$

$$C'(t) = I(t) + \lambda D(t) - (\nu + \delta + \mu + \gamma)\, C(t) \tag{9}$$

C(t) = Number of diabetics with complications

N(t) = Number of diabetics with and without complications

I = I(t) = Incidence rate of diabetes.

Table 1: Table of Definition of Parameters and Hypothetical Values

Parameter	Definition of Parameter	Values
δ	mortality rate due to complications	0.05
λ	probability of developing a complication	0.66
v	rate at which patients with complications become severely disabled	*0.05*
γ	rate at which complications are cured	0.08
μ	natural mortality rate	0.02
I	Incidence rate of diabetes mellitus	6 x 106

4. STABILITY ANALYSIS

Critical Point and Stability Criteria

Finding the critical point when

$$C'(t) = N'(t) = 0 \tag{10}$$

$$0 = I(t) - (\lambda + \theta)\, C(t) + \lambda N(t) \tag{11}$$

$$0 = 2I(t) - (v + \delta)\, C(t) - \mu N(t) \tag{12}$$

Solving simultaneously and simplifying we obtained

$$C^*(t) = \frac{(2\lambda + \mu)I(t)}{v\lambda + \mu\theta + \lambda\delta + \lambda\mu} \tag{13}$$

$$N^*(t) = \frac{(2(\lambda + \theta) - (\mu + \delta))I(t)}{v\lambda + \mu\theta + \lambda\delta + \lambda\mu} \tag{14}$$

where C*(t) and N*(t) are critical-point values of C(t) and N(t).

C*(t) = 96,643.38, N*(t) = 116,826,923.077

Finding the Eigenvalues

$$\begin{pmatrix} C(t) \\ N(t) \end{pmatrix} = \begin{pmatrix} -(\lambda + \theta) & \lambda \\ -(v + \delta) & -\mu \end{pmatrix} \begin{pmatrix} C(t) \\ N(t) \end{pmatrix} + \begin{pmatrix} I(t) \\ 2I(t) \end{pmatrix} \tag{15}$$

The characteristic matrix is

$$\begin{vmatrix} -(\lambda + \theta) - \kappa & \lambda \\ -(v + \delta) & -\mu - \kappa \end{vmatrix} = 0 \tag{16}$$

where κ is a scalar (Eigenvalues).

The characteristic equation is

$$(\lambda + \theta + \kappa)\,(\mu + \kappa) + \lambda(v + \delta) = 0 \tag{17}$$

$\kappa^2 + 0.88\kappa + 0.0832 = 0$ (18)

$\kappa_1 = -0.1077$ and $\kappa_2 = -0.7722$

Since the Eigenvalues are real, unequal and negative, the critical point is asymptotically stable.

5. THE EXACT SOLUTION

Our model equation is

$C'(t) = I(t) - (\lambda + \theta) C(t) + \lambda N(t) \quad C(0) = C_0$ (19)

$N'(t) = 2I(t) - (\nu + \delta) C(t) - \mu N(t) \quad N(0) = N_0$ (20)

Differentiating (19) gives

$C''(t) = -(\lambda + \theta) C'(t) + \lambda N'(t)$ (21)

Substituting (19), (20) into (21) result to

$C''(t) = [(\lambda + \theta)^2 - \lambda(\nu + \delta)] C(t) - \lambda(\lambda + \theta + \mu) N(t) + (\lambda - \theta) I(t)$ (22)

From (19)

$N(t) = \frac{1}{\lambda}(C'(t) - I(t) + (\lambda + \theta) C(t))$ (23)

Substituting (23) into (22) gives

$C''(t) = -(\lambda + \theta + \mu)C'(t) + (2\lambda + \mu) I(t) + ((\lambda + \theta)^2 - \lambda(\nu + \delta) - (\lambda + \theta + \mu)(\lambda + \theta)) C(t)$ (24)

$C''(t) = -(\lambda + \theta + \mu)C'(t) + (2\lambda + \mu) I(t) - (\lambda\nu + \lambda\delta + \lambda\mu + \mu\theta) C(t)$ (25)

Hence we obtained

$C''(t) + \sigma C'(t) + \beta C(t) = \alpha I(t)$ (26)

where

$\sigma = \lambda + \theta + \mu$ (27)

$\beta = \lambda\nu + \lambda\delta + \lambda\mu + \mu\theta$ (28)

$\alpha = 2\lambda + \mu$ (29)

The auxilliary equation for the homogenous part of (26) is

$m^2 + \sigma m + \beta = 0$ (30)

Solving the quadratic equation (30), we have

$$m = \frac{-\sigma \pm \sqrt{\sigma^2 - 4\beta}}{2}$$

The complimentary solution of (26) is

$$C(t) = K_1 e^{-1/2(\sigma - \sqrt{\sigma^2 - 4\beta})t} + K_2 e^{-1/2(\sigma + \sqrt{\sigma^2 - 4\beta})t}$$ (31)

Using the method of undetermined coefficient to find the particular integral (solution).

Let

$C_p(t) = K$ (32)

$C'_p(t) = 0$ (33)

$C''_p(t) = 0$ (34)

Substituting (32), (33) and (34) into (26) we obtained

$C_p(t) = \frac{\alpha}{\beta} I(t)$ (35)

The complete solution of (26) is

$C(t) = K_1 e^{-1/2(\sigma - \sqrt{\sigma^2 - 4\beta})t} + K_2 e^{-1/2(\sigma + \sqrt{\sigma^2 - 4\beta})t} + \frac{\alpha}{\beta} I(t)$ (36)

Let

$\eta_1 = \frac{1}{2}(\sigma - \sqrt{\sigma^2 - 4\beta})$

$\eta_2 = \frac{1}{2}(\sigma + \sqrt{\sigma^2 - 4\beta})$

$C(t) = K_1 e^{-\eta_1 t} + K_2 e^{-\eta_2 t} + \frac{\alpha}{\beta} I(t)$ (37)

$C'(t) = -(\eta_1 K_1 e^{-\eta_1 t} + \eta_2 K_2 e^{-\eta_2 t})$ (38)

Substituting (37) and (38) into (23), we have

$N(t) = K_1 e^{-\eta_1 t} + K_2 e^{-\eta_2 t} + \frac{\alpha}{\beta} I(t) + \frac{\theta}{\lambda} K_1 e^{-\eta_1 t} + \frac{\theta}{\lambda} K_2 e^{-\eta_2 t} + \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \frac{I(t)}{\lambda}$

$- \frac{1}{\lambda}(\eta_1 K_1 e^{-\eta_1 t} + \eta_2 K_2 e^{-\eta_2 t})$ (39)

Using the initial conditions on (37) and (39) and simplifying, we obtained

$K_1 = \frac{\beta(\lambda + \theta - \eta_2)C_0 + I(\alpha\eta_2 - \beta) - \lambda\beta N_0}{\beta(\eta_1 - \eta_2)}$ (40)

$K_2 = \frac{-\beta(\lambda + \theta - \eta_1)C_0 + I(\beta - \alpha\eta_1) + \lambda\beta N_0}{\beta(\eta_1 - \eta_2)}$ (41)

7. LIMITING CASE BEHAVIOUR

Taking the limit of the solution

- Limit at infinity

- $\lambda \to \infty$

$$\lim_{\lambda\to\infty} C(t) = \lim_{\lambda\to\infty} K_1 e^{-\eta 1 t} + \lim_{\lambda\to\infty} K_2 e^{-\eta 2 t} + \lim_{\lambda\to\infty} \frac{\alpha}{\beta} I(t)$$

$$= K_1 \times 0 + K_2 \times 0 + \lim_{\lambda\to\infty} \frac{2\lambda + \mu}{(\lambda\nu + \lambda\delta + \lambda\mu + \mu\theta)} I(t)$$

$$\lim_{\lambda\to\infty} C(t) = \frac{2 I(t)}{\nu + \delta + \mu}$$

$$\lim_{\lambda\to\infty} N(t) = \lim_{\lambda\to\infty} K_1 e^{-\eta 1 t} + \lim_{\lambda\to\infty} K_2 e^{-\eta 2 t} + \lim_{\lambda\to\infty} \frac{\alpha}{\beta} I(t)$$

$$+ \lim_{\lambda\to\infty} \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \lim_{\lambda\to\infty} \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \lim_{\lambda\to\infty} \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \lim_{\lambda\to\infty} \frac{I(t)}{\lambda}$$

$$- \lim_{\lambda\to\infty} \frac{1}{\lambda} (\eta 1 K1 e^{-\eta 1 t} + \eta 2 K2 e^{-\eta 2 t})$$

$$\lim_{\lambda\to\infty} N(t) = \frac{2 I(t)}{\nu + \delta + \mu}$$

- $\gamma \to \infty$

$$\lim_{\gamma\to\infty} C(t) = \lim_{\gamma\to\infty} K_1 e^{-\eta 1 t} + \lim_{\gamma\to\infty} K_2 e^{-\eta 2 t} + \lim_{\gamma\to\infty} \frac{\alpha}{\beta} I(t)$$

$$= K_1 \times 0 + K_2 \times 0 + \lim_{\gamma\to\infty} \frac{2\lambda + \mu}{(\lambda\nu + \lambda\delta + \lambda\mu + \mu\theta)} I(t)$$

$$\lim_{\gamma\to\infty} C(t) = \frac{0}{\mu} = 0$$

$$\lim_{\gamma\to\infty} N(t) = \lim_{\gamma\to\infty} K_1 e^{-\eta 1 t} + \lim_{\gamma\to\infty} K_2 e^{-\eta 2 t} + \lim_{\gamma\to\infty} \frac{\alpha}{\beta} I(t)$$

$$+ \lim_{\gamma\to\infty} \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \lim_{\gamma\to\infty} \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \lim_{\gamma\to\infty} \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \lim_{\gamma\to\infty} \frac{I(t)}{\lambda}$$

$$- \lim_{\gamma\to\infty} \frac{1}{\lambda} (\eta 1 K1 e^{-\eta 1 t} + \eta 2 K2 e^{-\eta 2 t})$$

$$\lim_{\gamma\to\infty} N(t) = \frac{2 I(t)}{\mu}$$

- $\delta \to \infty$

$$\lim_{\delta\to\infty} C(t) = \lim_{\delta\to\infty} K_1 e^{-\eta 1 t} + \lim_{\delta\to\infty} K_2 e^{-\eta 2 t} + \lim_{\delta\to\infty} \frac{\alpha}{\beta} I(t)$$

$$= K_1 \times 0 + K_2 \times 0 + \lim_{\delta \to \infty} \frac{(2\lambda + \mu)}{(\lambda\nu + \lambda\delta + \lambda\mu + \mu\delta + \mu\gamma + \nu\mu + \mu^2)} I(t)$$

$$\lim_{\delta \to \infty} C(t) = \frac{0}{\lambda + \mu} = 0$$

$$\lim_{\delta \to \infty} N(t) = \lim_{\delta \to \infty} K_1 e^{-\eta 1 t} + \lim_{\delta \to \infty} K_2 e^{-\eta 2 t} + \lim_{\delta \to \infty} \frac{\alpha}{\beta} I(t)$$

$$+ \lim_{\delta \to \infty} \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \lim_{\delta \to \infty} \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \lim_{\delta \to \infty} \frac{\theta}{\lambda} \frac{\alpha}{\beta} I(t) - \lim_{\delta \to \infty} \frac{I(t)}{\lambda}$$

$$- \lim_{\delta \to \infty} \frac{1}{\lambda} (\eta 1 K1 e^{-\eta 1 t} + \eta 2 K2 e^{-\eta 2 t})$$

$$\lim_{\delta \to \infty} N(t) = \lim_{\delta \to \infty} \frac{\alpha}{\beta} I(t) + \lim_{\delta \to \infty} \frac{\theta}{\lambda} \frac{\alpha}{\beta} I(t) - \lim_{\delta \to \infty} \frac{I(t)}{\lambda}$$

$$\lim_{\delta \to \infty} N(t) = \frac{0}{\lambda + \mu} + \frac{(2\lambda + \mu) I(t)}{\lambda(\lambda + \mu)} - \frac{I(t)}{\lambda}$$

$$\lim_{\delta \to \infty} N(t) = \frac{I(t)}{\lambda + \mu}$$

- $\nu \to \infty$

$$\lim_{\nu \to \infty} C(t) = \lim_{\nu \to \infty} K_1 e^{-\eta 1 t} + \lim_{\nu \to \infty} K_2 e^{-\eta 2 t} + \lim_{\nu \to \infty} \frac{\alpha}{\beta} I(t)$$

$$\lim_{\nu \to \infty} C(t) = \lim_{\nu \to \infty} \frac{\alpha}{\beta} I(t) = \lim_{\nu \to \infty} \frac{(2\lambda + \mu)}{(\lambda\nu + \lambda\delta + \lambda\mu + \mu\delta + \mu\gamma + \nu\mu + \mu^2)} I(t)$$

$$\lim_{\nu \to \infty} C(t) = \frac{0}{\lambda + \mu} = 0$$

$$\lim_{\nu \to \infty} N(t) = \lim_{\nu \to \infty} K_1 e^{-\eta 1 t} + \lim_{\nu \to \infty} K_2 e^{-\eta 2 t} + \lim_{\nu \to \infty} \frac{\alpha}{\beta} I(t)$$

$$+ \lim_{\nu \to \infty} \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \lim_{\nu \to \infty} \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \lim_{\nu \to \infty} \frac{\theta}{\lambda} \frac{\alpha}{\beta} I(t) - \lim_{\nu \to \infty} \frac{I(t)}{\lambda}$$

$$- \lim_{\nu \to \infty} \frac{1}{\lambda} (\eta 1 K1 e^{-\eta 1 t} + \eta 2 K2 e^{-\eta 2 t})$$

$$\lim_{\nu \to \infty} N(t) = \lim_{\nu \to \infty} \frac{\alpha}{\beta} I(t) + \lim_{\nu \to \infty} \frac{\theta}{\lambda} \frac{\alpha}{\beta} I(t) - \lim_{\nu \to \infty} \frac{I(t)}{\lambda}$$

$$\lim_{\nu \to \infty} N(t) = \frac{0}{\lambda + \mu} + \frac{(2\lambda + \mu) I(t)}{\lambda(\lambda + \mu)} - \frac{I(t)}{\lambda}$$

$$\lim_{\nu \to \infty} N(t) = \frac{I(t)}{\lambda + \mu}$$

- **Limit at Zero**
- $\lambda \to 0$

$$\lim_{\lambda\to 0} C(t) = \lim_{\lambda\to 0} K_1 e^{-\eta 1 t} + \lim_{\lambda\to 0} K_2 e^{-\eta 2 t} + \lim_{\lambda\to 0} \frac{\alpha}{\beta} I(t)$$

$$\lim_{\lambda\to 0} C(t) = C_0 e^{-\theta t} + \frac{I(t)}{\theta}(1- e^{-\theta t})$$

$$\lim_{\lambda\to 0} N(t) = \lim_{\lambda\to 0} K_1 e^{-\eta 1 t} + \lim_{\lambda\to 0} K_2 e^{-\eta 2 t} + \lim_{\lambda\to 0} \frac{\alpha}{\beta} I(t)$$

$$+ \lim_{\lambda\to 0} \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \lim_{\lambda\to 0} \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \lim_{\lambda\to 0} \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \lim_{\lambda\to 0} \frac{I(t)}{\lambda}$$

$$\lim_{\lambda\to 0} N(t) = \infty$$

where, as $\lambda \to 0$, then

$$\lim_{\lambda\to 0} \theta = \lim_{\lambda\to 0} (\gamma + \mu + \nu + \delta) = \theta$$

$$\lim_{\lambda\to 0} \beta = \lim_{\lambda\to 0} (\lambda\nu + \lambda\delta + \lambda\mu + \mu\theta) = \theta\mu$$

$$\lim_{\lambda\to 0} \alpha = \lim_{\lambda\to 0} (2\lambda + \mu) = \mu$$

$$\lim_{\lambda\to 0} \sigma = \lim_{\lambda\to 0} (\lambda + \theta + \mu) = \theta + \mu$$

$$\lim_{\lambda\to 0} \eta_1 = \lim_{\lambda\to 0} \left(\frac{1}{2}\left(\sigma - \sqrt{\sigma^2 - 4\beta}\right)\right) = \mu$$

$$\lim_{\lambda\to 0} \eta_2 = \lim_{\lambda\to 0} \left(\frac{1}{2}\left(\sigma + \sqrt{\sigma^2 - 4\beta}\right)\right) = \theta$$

$$\lim_{\lambda\to 0} K_1 = \lim_{\lambda\to 0} \left(\frac{\beta(\lambda + \theta - \eta 2) C_0 + I(\alpha\eta 2 - \beta) - \lambda\beta N_0}{\beta(\eta 1 - \eta 2)}\right) = 0$$

$$\lim_{\lambda\to 0} K_2 = \lim_{\lambda\to 0} \left(\frac{-\beta(\lambda + \theta - \eta 1) C_0 + I(\beta - \alpha\eta 1) + \lambda\beta N_0}{\beta(\eta 1 - \eta 2)}\right) = C_0 - \frac{I(t)}{\theta}$$

- $\gamma \to \infty, \lambda \to 0$

$$\lim_{\gamma\to\infty}\lim_{\lambda\to 0} C(t) = \lim_{\gamma\to\infty}\left(C_0 e^{-\theta t} + \frac{I(t)}{\theta}(1- e^{-\theta t})\right)$$

$$= \lim_{\gamma\to\infty} \frac{I(t)}{\theta} = \lim_{\gamma\to\infty} \frac{I(t)}{(\gamma + \mu + \nu + \delta)} = 0$$

$$\lim_{\gamma\to\infty}\lim_{\lambda\to 0} N(t) = \infty$$

- $\gamma \to 0$

$$\lim_{\gamma\to 0} C(t) = \lim_{\gamma\to 0} K_1 e^{-\eta 1 t} + \lim_{\gamma\to 0} K_2 e^{-\eta 2 t} + \lim_{\gamma\to 0} \frac{\alpha}{\beta} I(t)$$

$$\lim_{\gamma\to 0} C(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{\theta(\lambda+\mu)} I(t)$$

$$\lim_{\gamma\to 0} N(t) = \lim_{\gamma\to 0} K_1 e^{-\eta 1 t} + \lim_{\gamma\to 0} K_2 e^{-\eta 2 t} + \lim_{\gamma\to 0} \frac{\alpha}{\beta} I(t) + \lim_{\gamma\to 0} \frac{\theta}{\lambda} K_1 e^{-\eta 1 t}$$

$$+ \lim_{\gamma\to 0} \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \lim_{\gamma\to 0} \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \lim_{\gamma\to 0} \frac{I(t)}{\lambda}$$

$$- \lim_{\gamma\to 0} \frac{1}{\lambda} (\eta_1 K_1 e^{-\eta 1 t} + \eta_2 K_2 e^{-\eta 2 t})$$

$$\lim_{\gamma\to 0} N(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{\theta(\lambda+\mu)} I(t) + \frac{\theta}{\lambda} K_1 e^{-\eta 1 t}$$

$$+ \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{\lambda(\lambda+\mu)} I(t) - \frac{I(t)}{\lambda} - \frac{1}{\lambda}(\eta_1 K_1 e^{-\eta 1 t}) - \frac{1}{\lambda}(\eta_2 K_2 e^{-\eta 2 t})$$

where, as $\gamma \to 0$, then

$$\lim_{\gamma\to 0} \theta = \lim_{\gamma\to 0} (\gamma + \mu + \nu + \delta) = (\mu + \nu + \delta)$$

$$\lim_{\gamma\to 0} \beta = \lim_{\gamma\to 0} (\lambda\nu + \lambda\delta + \lambda\mu + \mu\theta) = \theta (\lambda + \mu)$$

- $\delta \to 0$

$$\lim_{\delta\to 0} C(t) = \lim_{\delta\to 0} K_1 e^{-\eta 1 t} + \lim_{\delta\to 0} K_2 e^{-\eta 2 t} + \lim_{\delta\to 0} \frac{\alpha}{\beta} I(t)$$

$$\lim_{\delta\to 0} C(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{(\nu+\mu)(\lambda+\mu)+\mu\gamma} I(t)$$

$$\lim_{\delta\to 0} N(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{\alpha}{\beta} I(t) + \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) \quad \frac{I(t)}{\lambda} - \frac{1}{\lambda}(\eta_1 K_1 e^{-\eta 1 t}$$

$$+ \eta_2 K_2 e^{-\eta 2 t})$$

where, as $\delta \to 0$, then

$$\lim_{\delta\to 0} \theta = \lim_{\delta\to 0} (\gamma + \mu + \nu + \delta) = (\gamma + \mu + \nu)$$

$$\lim_{\delta\to 0} \beta = \lim_{\delta\to 0} (\lambda\nu + \lambda\delta + \lambda\mu + \mu\theta\&) = (\nu + \mu)(\lambda + \mu) + \mu\gamma$$

- $\gamma \to \infty$, $\lambda \to 0, \delta \to 0$

$$\lim_{\gamma\to\infty}\lim_{\lambda\to 0}\lim_{\delta\to 0} C(t) = \lim_{\gamma\to\infty}\lim_{\lambda\to 0}(K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t})$$

$$+\lim_{\gamma\to\infty}\lim_{\lambda\to 0}(\frac{(2\lambda+\mu)}{(\nu+\mu)(\lambda+\mu)+\mu\gamma} I(t)) = 0$$

$$\lim_{\gamma\to\infty}\lim_{\lambda\to 0}\lim_{\delta\to 0} N(t) = \lim_{\gamma\to\infty}\lim_{\lambda\to 0}(K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{\alpha}{\beta} I(t))$$

$$+\lim_{\gamma\to\infty}\lim_{\lambda\to 0}(\frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \frac{I(t)}{\lambda})$$

$$\lim_{\gamma\to\infty}\lim_{\lambda\to 0} -\frac{1}{\lambda}(\eta_1 K_1 e^{-\eta 1 t} + \eta_2 K_2 e^{-\eta 2 t}) = \infty$$

8. DISCUSSION AND INTERPRETATION OF THE LIMITING CASES BEHAVIOUR

The following discussion and interpretation are based on the result of the limiting cases:

- If the probability of developing a complication is very high ($\lambda \to \infty$), that is, if it almost sure that a diabetic will develop a complication, which may result from inadequate control of glucose level in the blood. Then the number of diabetic with and without complications will be the same with the number of diabetics with complications. This translates to need for regular check of the blood glucose level for early detection and timely control.
- With very high rate at which complications of diabetes are cured ($\gamma \to \infty$), the number of diabetics with complications will eventually reduce to zero while the total number of diabetics will depend directly on incidence of diabetes and indirectly on the natural mortality rate.

This translates to the need to intensify effort to combat the complications of diabetes mellitus and reduce its incidence.

- When the mortality rate due to complications is very high ($\delta \to \infty$), that is, the rate at which complications are cured is slow. The number of diabetics with complications reduces to zero. This may be due to late diagnosis, poor and inadequate health care delivery and overall treatment which eventually leads to untimely death. The total number of diabetics will depend on the incidence and the probability of developing complications.
- When the rate at which patients with complications become severely disabled is very high ($\nu \to \infty$), the number of diabetics with complications approaches zero. This may be because severe disability leads to untimely death.

The number of diabetics then stands at $\frac{I(t)}{\lambda+\mu}$ .This translates to the need to intensify effort to reduce incidence of diabetes mellitus and its attendant complications.

- When the likelihood of developing a complication approaches zero (is reducing) ($\lambda \to 0$), the number of diabetics with complications stabilizes at

$$C_0 e^{-\theta t} + \frac{I(t)}{\theta}(1- e^{-\theta t})$$

This may be due to a thorough preventive and treatment programme. But the number of diabetics will still

increase without bound.

- When the probability of developing a complication tends to zero,($\lambda \to 0$) and the rate at which complications are cured is very high,($\gamma \to \infty$) the number of diabetics without complications drops to zero while the number of diabetics increases without bound.

- When the rate at which complications are cured approaches zero (is reducing), ($\gamma \to 0$), the value of C(t) and N(t) stand as given below

$$C(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{\theta(\lambda+\mu)} I(t)$$

$$N(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{\theta(\lambda+\mu)} I(t) + \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{\lambda(\lambda+\mu)} I(t) - \frac{I(t)}{\lambda} - \frac{1}{\lambda}(\eta_1 K_1 e^{-\eta 1 t}) - \frac{1}{\lambda}(\eta_2 K_2 e^{-\eta 2 t})$$

- When the mortality rate due to complications tends to zero, (is reducing) ($\delta \to 0$). This may be as a result of intensive and comprehensive recovery programme. The value of C(t) and N(t) reduce to the definite values given below

$$C(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{(2\lambda+\mu)}{(\nu+\mu)(\lambda+\mu)+\mu\gamma} I(t)$$

$$N(t) = K_1 e^{-\eta 1 t} + K_2 e^{-\eta 2 t} + \frac{\alpha}{\beta} I(t) + \frac{\theta}{\lambda} K_1 e^{-\eta 1 t} + \frac{\theta}{\lambda} K_2 e^{-\eta 2 t} + \frac{\theta}{\lambda}\frac{\alpha}{\beta} I(t) - \frac{I(t)}{\lambda} - \frac{1}{\lambda}(\eta_1 K_1 e^{-\eta 1 t} + \eta_2 K_2 e^{-\eta 2 t})$$

9) With very high rate of recovery from complications $(\gamma \to \infty)$, probability of developing a complication decreasing ($\lambda \to 0$) and mortality rate due to complication approaching zero($\delta \to 0$), the number of diabetics with complications reduces to zero while the total number of diabetics increases without bound. Hence the need to reduce the incidence of diabetes and improve on the treatment of those with complications.

CONCLUSIONS

In this paper, the model aided the understanding of diabetes, its complications and how it can be controlled. We investigated the stability of the equilibrium point and found it to be asymptotically stable. This suggests that the complications of diabetes mellitus can be controlled. Also, investigating the limiting case behaviour of each parameter in the analytic solution of the model depicts that if some measures are taken the number of diabetics with complications will be reduced to the bearest minimum.

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